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09/910,071	07/23/2001	Mayumi Tomikawa	522.1921D2	2943

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EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/910,071

Applicant(s)

TOMIKAWA ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07/05/2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-15 and 24-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-15 and 24-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of Claims

1. Claims 13-15, 24-26 are pending. Claims 13,24 are amended.

Rejections not reiterated from previous Office actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 13-15, 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons.

B. Claims 13,24 are amended to add the final step of concluding that the functions of two structures are substantially equivalent. The meaning of the term "function" of "sequences of atoms" or of "atomic groups" of biological molecules is not clear, the specification does not define the term and it is not clear what kind of function(s) is being defined based on similarity of 3-D coordinates. For example, if 3-D coordinates of a

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phosphate group (i.e., "atomic group") in a nucleic acid correlates with 3-D coordinates of a phosphate group in a lipid or a protein, what kind of function is determined to be "substantially equivalent".

Further, it is not clear what constitutes a "function" for a "sequence of atoms" or for "a sequence of atomic groups".

Response to arguments

Applicant cites section of specification (p. 5-6) discussing that a determining a "structure common among heat resistant substances" (is there a structure common among all heat resistant substances?) allows to produce a new product. Further, this section states that "function is required to retrieve the necessary structure from database". It is not clear how discussion of these issues is related to the issue of ambiguity of the term "function" of "sequences of atoms" or of "atomic groups" of biological molecules, as it is used in the context of the claimed invention. Likewise, the dictionary definition of a function as "action for which a person or thing is specially fitted" does not resolve the ambiguity of the term "function" of "sequences of atoms" or of "atomic groups"

Specification does not provide a standard for ascertaining the meaning of the term "function", and one of ordinary skills in the art would not be reasonably appraised of the scope of the invention.

With respect to the question what constitutes a "function" for a "sequence of atoms" or for "a sequence of atomic groups", applicant argues that a function for a sequence of atoms is understood by one skilled in the art. Examiner disagrees. What function will be understood, e.g., for a sequence of C-C-C-N atoms? Further, even for

known sequences of amino acids in polypeptides (rather than sequences of atoms) assigning a function by comparing structures is questionable. See discussion in utility rejection below.

Claim Rejections - 35 USC § 101 (utility)

3. Claims 13-15, 24-26 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The rejection is maintained for the reasons of record and further in view of the following:

The instant claims are drawn to a computer process whereby, based on similarity in 3-D structures of "sequences of atoms" or of "atomic groups" of biological molecules, a determination is made whether a function of the first "sequences of atoms" or "atomic group" is equivalent to a function of the second "sequences of atoms" or "atomic group". The claims do not recite any particular function or any other practical application of the method. Specification does not specify what kind of "function" is related to a 3-D structure of "sequences of atoms" or "atomic group".

According to MPEP 2107.01 and as set forth in *Brenner v. Manson* (148 USPQ 689 (1966)) and *In re Ziegler* (26 USPQ 2d 1600), a "useful invention" is one wherein the "usefulness" is "immediately apparent to those familiar with the technological field of the invention. As further set forth in MPEP 2107.01, a "use" to do further research, is not considered a "substantial utility" under 35 USC 101. As the structures being "assayed"

are unknown/not identified in the claim, their utility is unknown. Neither a "function" correlated with the three-dimensional structure is identified. Thus, it is

Examiner maintains the claimed invention does not have a substantial utility as more information and/or further research would be required for one skilled in the art to identify what particular functions of "sequences of atoms" or "atomic group" are related to a 3-D structure of said "sequences of atoms" or "atomic group".

Applicant argues that "for specific amino acid sequences, certain functions are known". However, the instant claims do not address "specific amino acid sequence"; rather, the claims are directed to undefined "sequences of atoms" or "atomic group" (of previously unknown compounds) and their equally undefined "functions".

Applicant discusses Fig. 42 and section in specification describing it (p. 56-57). However, this discussion is unrelated to the issue of the lack of nexus between similarity in 3-D structure of "sequences of atoms" or "atomic group" and an unidentified function thereof.

Even if the discussion of utility is to be limited to analyzing of 3D structures of polypeptides (rather than "sequences of atoms" or "atomic group"), such comparison is a result which lacks substantial utility as subsequent research is needed to identify the utility of finding such 3D similarities. Thus, Zu-Kang (Folding and Design , 1, 123-132, 1996) teaches that studies based on superimposition of 3D structures are "bound to be misleading" (end of Abstract). Zu-Kang discusses that structure/structure alignments are often used in the analysis of conserved features of protein folds but

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conclusions deriving from such studies can be misleading, as structure alignments are ambiguous. (p. 129).

There is a prevailing tenet that protein structures are more conserved than sequences. This requires that such structurally conserved pairs can be identified in a unique fashion. When alternative alignments exist which are indistinguishable in geometric terms, this task becomes difficult or impossible unless additional criteria are available that allow us to discriminate the set of evolutionarily related residue pairs from those pairs that are only geometrically equivalent. Examples of such additional features that could be used to identify conserved residues are a significant number of residue identities in one alignment or a match of functional residues. However, most sets of alternative alignments found in this study are indistinguishable by these criteria and further investigation of this issue will be an interesting exercise. In any case, protein pairs that can be aligned in alternative ways are the rule rather than exceptions (Table 1) and unresolvable ambiguities in structural similarity support the argument in favour of convergent rather than divergent evolution. (p. 128-129)

Thus, even if the claimed method provided determining degree of spatial similarity for polypeptides, identification of significance of the determined similarity with respect to a "function" would require further research. As such, the claimed method lacks substantial utility.

4. Claims 13-15, 24-26 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 101 (non-statutory)

5. Claims 13-15, 24-26 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The rejection is applied for the reasons of record and further in view of the following.

The instant claims are drawn to a computer process whereby, based on similarity in 3-D structures of "sequences of atoms" or of "atomic groups" of biological molecules, a determination is made whether a function of the first "sequences of atoms" or "atomic group" is equivalent to a function of the second "sequences of atoms" or "atomic group".

Applicant argues that such determination constitutes a useful result. However, as discussed in the utility rejection above, the method as claimed lacks substantial utility. Further, if a claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory. In the instant case, even though applicant addresses potential functions of amino acid sequences, the claims encompass determining function of "sequences of atoms" or "atomic group". Thus, the claim encompasses determining "function" of e.g., such sequence of atoms as C-C-O-P, or C-C-C, or atomic group such as CH₃ (i.e., groups of atoms or atomic groups which are unlikely to have a meaningful "function"). Therefore, the claims are broader than the statutory embodiments of the claim which might have had a potential utility.

With respect to "tangible" criteria, the claim must set forth a practical application of the invention that produces a real-world result. Applicant argues that "determining a family of proteins to which a sequence belongs enables one to ascertain the properties of the sequence", which produces a real world, tangible result. However, the claims are neither to sequences amino acids (rather to "sequences of atoms" or "atomic group"), nor to determining families of proteins to which a sequence belongs. Further, the claims

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do not specify determination regarding which "function" is being made, and there is no evidence that such determination regarding an unidentified function produces a real-world result.

Taken together, the claims are directed to non-statutory subject matter as the claimed invention does not "transform" an article or physical object to a different state or thing, and the final result achieved by the claimed invention does not satisfy all three criteria of being useful, and concrete, and tangible.

Claim Rejections - 35 USC § 102.

6. Claims 13-15, 24-26 are rejected under 35 U.S.C. 102(b) as anticipated by Flaherty et al. (Proc. Natl. Acad. Sci. USA, 88, 5041-5045, 1991) or Mosimann et al.

The rejections are maintained for the reasons and in view of the following.

As before, the way applicant presents argument that the references do not teach the claimed invention is by providing full text of the instant claims. This makes it difficult to identify which particular limitation, in the opinion of the applicant, is not taught by the references. Therefore, Examiner attempts to address those sections of applicant's arguments which are emphasized by underlining.

It appears that applicant argues that the difference of the claimed method is that it is carried by a computer, whereas Flaherty uses manual steps, such as superimposition and inspecting. First, the reference is also directed to a computational

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method. Second, if there are any steps that seem to be more computerized in the instant method, broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art. In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958).

The underlined argument that the reference uses one letter codes to identify correspondence between residues – the argument follows citation of the claimed step of determining if degree of spatial similarity is greater than predetermined threshold - is not understood. Flaherty teaches that the structures are spatially equivalent if they can be superimposed within the predetermined r.m.s.d. (see Abstract).

On p. 20, applicant asserts that Faherty does not calculate rmsd to determine similarity of amino acid sequences. Applicant's attention is directed to abstract and p. 5042, section "Comparison of structures".

With respect to Mosimann et al reference, applicant also argues that the reference uses manual alignment using inspection by eye, compared to analyzing by computer processor in the instant method. Fig. 1, however, exemplifies analyzing three-dimensional structures by computer processor. Applicant also appears to argue that Mosimann uses structures that "have already been obtained". Examiner considers structures analyzed in the instant method as such that also "have already been obtained".

With respect to the use of rmsd only to confirm alignment, rather than to use it as a predetermined threshold, Examiner submits that the referenced method does both –

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see p. 395, first paragraph, for example, describing that distance of 2.6. A was set as arbitrary threshold to consider spatial similarity.

Examiner maintains that as the instant claims are drawn to method of analyzing three-dimensional structures by generating correspondence between set points describing two three-dimensional structures and calculating root mean square distance (rmsd) between the corresponding elements, the claims read on any reference teaching comparison of two three dimensional structures and calculating rmsd therefor. The references used in the rejection are exemplary of this commonly used approach to comparing of 3-D structures.

The rejection is maintained.

Double Patenting

7. Claims 13-15, 24-26 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16,17 of co-pending application 09/909809 or claims 5-11,24 of co-pending application 09/910054. The referenced claims of both applications are drawn to methods of analyzing three-dimensional structures including steps of dividing points, generating correspondences and calculating rmsd, as instantly claimed.

Applicant responds that the rejection is "premature". Note, that as was stated in the rejection, the rejection is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Prior art made of record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Lackner et al (Lackner et al. Protein Engineering, Vol. 13, No. 11, 745-752, 2000) describes method of finding 3D similarities between protein structures using ProSup algorithm which determines segments that can fit under RMSD cutoff.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

 Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631

mlb